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DISEASES OF THE NERVOUS SYSTEM

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Psychological Changes During Experimental Sleep Deprivation

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With the exceptions of the effect on the electrical activity of the brain[7] and the psychological disturbances,[1,3,6] very few other significant physiological, psychomotor or biochemical changes are found to occur during experimental deprivation of sleep for periods up to 112 hours.[2,3,6,8] Heavy work capacity, psychomotor skills (provided the tests do not require sustained attention), blood sugar, alkaline reserve, hemoglobin, red and white cell count, body weight, basal metabolism and body temperature show little variation from the normal. Even the urinary excretion of 17-ketosteroids is little affected by such stress and the slight change that occurs is a decrease rather than an increase.[8]

The changes in the EEG commence between 36 and 50 hours of wakefulness and are characterized principally by an increase in the time occupied by waves of higher frequencies. Also, a mental multiplication problem which causes an increase in the electrical activity of the brain of the normal rested subject produces little, or no, increase in the rate in the sleepless man.[7]

The psychological disturbances produced have been noted by other investigators.[1,3] In one series of studies a number of psychotic episodes occurred that resembled in many ways acute schizophrenia.[6] This report, therefore, is concerned with the frequency and severity of different psychological aberrations in male subjects who went without sleep for periods up to 112 hours. The results indicate that the prolonged deprivation of sleep causes an unknown organic disturbance of the higher centers of the central nervous system which produces, in practically all subjects, psychotic-like reactions. The difference in these reactions among the subjects is essentially one of degree.

Methods

Subjects

These studies were made on volunteers from army, marine corps, or civilian public service camps during the period from 1942 to 1946. They ranged in age from 17 to 35 years. All were informed as to the nature and purpose of the study, except in those details that might influence the results, such as the type of medication to be employed, etc. It was emphasized that they were free to drop out at any time and, if they did drop out, they were assured that it would not reflect in any way on their mliitary record. Therefore, when a man expressed such a desire, no effort was made to induce him to continue. However, there was considerable motivation for volunteering: freedom from routine training and work; on completing an

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Part of this paper was presented at the panel on "Scientific Approaches to Problems in Psychiatry" at the Annual Meeting of the American Psychiatric Association, Atlantic City, May, 1955

experiment it was understood that an extra 72 hours' leave would be granted; also they were the objects of admiration of the non-participating men in camp. In general, the morale was excellent, the volunteers were very cooperative and intelligent and were in sympathy with the purpose of the study—which was to test the effects of certain anti-fatigue agents under conditions of extreme fatigue, as well as to find out whether certain constituents of anti-motion sickness preparations would have an adverse effect on men who might be forced to remain awake for prolonged periods of time after taking such drugs.

Procedure

The work program, diet, medication, test situation, type of testing procedure employed, means of supervision and control of the subjects are described in detail elsewhere.[5,6] In all experiments the subjects worked together as a unit under the constant supervision of one or more observers. To study the effect of drugs the men were randomly divided into subgroups. Those that received amphetamine sulfate commenced taking 5 to 10 mgms. every 8 hours *after* they were awake for 48 hours; during the first 48 hours they were given placebos. Those given amytal, or a thiobarbiturate designated as "V-12,"[6] took the drugs for the first 48 hours. The dosage for amytal was 130 mgms. every 12 hours; for the thiobarbiturate, it ranged from 190 to 325 mgms. every 12 hours. After the 48th hour these men were given placebos. In every experiment one subgroup received only placebos throughout the entire period of sleeplessness.

The data reported here were obtained from 8 experiments of 112 hours' duration, involving a total of 350 men.

Results

The psychic changes that occurred during these studies are grouped, for convenience, as follows: 1) psychoneurotic-like; 2) schizophrenic-like reactions; 3) paranoid reactions. Except for the psychoneurotic, these reactions occurred in approximately the same frequency among the members of all subgroups irrespective of the medication given.

1. Psychoneurotic-like Reactions

Approximately 22 per cent of 350 volunteers (76 men) did not complete the experiment although there was considerable variation from experiment to experiment. For instance, in 2 experiments, one involving 48 men and the other 12, all men completed the 112 hours; in another experiment, with 75 starting, 23 dropped out by the 48th hour. The highest incidence of men quitting was in the period between the 20th to 48th hour. If a man showed any symptoms of illness such as fever, cold, etc., he was made to discontinue the experiment. Such factors accounted for about 40 per cent of the number not finishing. Included in this group are 7 subjects who developed emotional and psychic disturbances of such a nature as to warrant dropping them from the experiment. These cases are described below. The rest that quit (44 men) dropped out of their own volition and for reasons that may be classified as (a) anxiety, (b) psychosomatic complaints, (c) irritation.

a. Vague Fears or Mild Anxiety States

Included here are 19 men who gave reasons that indicated they were afraid the experiment was doing them harm. A number of them were concerned that they might lose the ability to sleep properly again. Some feared that they would "lose their mind"; others were worried about the effect on their records if they were to drop out later from the experiment. They were unconvinced that it would not be entered into their records if they were to make a poor showing. Over half of these individuals dropped out during the first 24 hours. It is not uncommon for men (and women) in the age group used in these studies to stay up all night on parties, in some instances for periods longer than the length of time they went without sleep in this experiment before quitting. When this was pointed out, some of them gave vague answers implying that the situations were different. It appeared that a substantial number of those who dropped out early in the experiment developed unreasonable and vague fears of continuing longer.

b. Psychosomatic Complaints

With a few exceptions there appeared little, or no, physical basis for the ailments

described. Most of those who exhibited mild anxiety states also had complaints about their health. Most frequent (20 instances) were headaches, "tight feeling" in head, "head hurts but it is not like headache." However, 2 subjects maintained that they were suffering from very severe headaches, which may have been migraine in nature, but neither one admitted having suffered from this disability before. It should be mentioned that headaches were not uncommon complaints among those who finished the experiment. Next frequent (15 men) were gastrointestinal complaints. Loss of appetite (generally not confirmed by observers at meals), stomach ache, diarrhea and constipation were frequent reasons given by men who wished to drop out of the experiment. Nausea, dizziness and feeling faint (but no indication of pallor) were also explanations offered by eight who dropped out early.

c. Irritation

Among those that dropped out of their own volition, there were a few that showed definite signs of increased irritability, particularly by the middle of the second day. They became uncooperative, a characteristic not noticeable when they had been selected from the volunteers for the study. (It should be noted that all subjects showed increased irritability with loss of sleep; this group, however, appeared more sensitive in this respect.) Three in this category suddenly quit the experiment without reporting to the observer. Since the men were free to drop out at any time they chose no pressure whatsoever was put on any of them to continue. Nevertheless, it was the general impression that nothing could have induced these men to continue.

It is of interest to note that in the subgroups taking amytal during the first 2 days, there was a loss of about 5 per cent of their number compared with 19 per cent for subgroups taking placebos.[6]

2. Schizophrenic-like Reactions

a. Illusions, Delusions and Hallucinations

These disturbances usually started after 40 hours without sleep. Over 70 per cent of all subjects, irrespective of whether they were taking medication or not, complained of auditory or visual aberrations. In the great majority they occurred periodically and, since the men were aware that they were hearing or seeing things that did not exist, they could not be classed as true hallucinations. The most common experiences concerned females: the subject saw a girl or female relative; fellow subjects on the experiments resembled girls. Next common were hallucinations involving animals—hearing dogs barking, or roosters crowing, or other animal sounds. Visual hallucinations of animals were reported by a number of subjects.

Four men, in addition to two others described below, experienced aberrations that appeared to be true hallucinations and their behavior was bizarre enough to drop them from the experiment. One insisted his mother and girl friend were watching him in the testing room and demanded that they be sent home. Another was quite disturbed, claiming that women were being used as examiners and demanding that they be discharged. One man constantly heard dogs barking; another started to talk to himself as if he were conversing with some unseen person. When this occurred a number of times, the latter was dropped and ordered to bed. Two other cases of hallucinations together with delusions will be described below under "paranoid reactions."

b. Disturbance in Thinking

This was common to all subjects after the second night, but it was most difficult to detect during the test situation. This period, devoted to formal testing, started at sundown and lasted for approximately 3½ hours. The results obtained from a wide variety of examinations designed to measure their ability to complete sentences, define and associate words, interpret stories, or solve elementary problems in logic, indicated that practically all subjects performed normally during this period (see 5, 6 for full details of tests employed). During the test situation there was no indication of disturbances in the sensorium or decrease in intellectual ability; they were well oriented and had no difficulty in retention or calculation. They made as good, or better, scores on the 3rd or 4th days on such tests as retention and recall of digits, both forward and reverse, and the Shipley-Hartford conceptual quotient.

There was some loss of memory as sleeplessness progressed but this was primarily for recent events occurring during the experiment. Comparison of Rorschach tests taken prior to an experiment and again after 100 hours of wakefulness showed no significant changes: approximately equal numbers of men showed either gains, losses or no change at the 100th hour.

There were, however, three cases which, on being examined during a test situation, exhibited some persistence in repeating an answer that had been given to a previous question. For instance, one subject on being asked the approximate time gave the answer correctly. Next he was asked how far he had marched that day. In answer he repeated the time. He was then asked his age. Again, he gave the time and then, suddenly, asked "What?", having become aware that something was amiss with his replies.

On the other hand, disturbances in thought processes were more apparent outside the test situation and during the spontaneous conversation of the subjects at meals, on marches, or during rest periods. Very common were rambling, garrulous speech with a lack of coherent structure or logical connection among the many ideas that were covered in a few minutes conversation. Frequently, there was difficulty in answering simple questions regarding common experiences or giving the name of another subject. For example, one man when asked on the 4th day at mess, "What is the name of the captain of your company?" answered after a moment, "He is married."

These disturbances in thinking occurred more frequently at night and lasted for short periods, usually until the subject himself became aware of his wandering thoughts and conversation. The phenomenon appeared wave-like and related to recurrent periods of extreme difficulty in keeping awake.

c. Unreasonable, Unrelated or Silly Laughter

Although data on this behavior was not recorded it happened often enough to be noticeable, usually while the man was performing some task rather than during the test situation. The laughing would occur for no apparent reason and, on questioning, the subject either did not know he had laughed or was surprised at being told he had. Occasionally, a man replied that he was thinking of a funny situation which, on inspection, did not seem reasonable enough to provoke the reaction.

d. Changes in Emotional Response

This was difficult to observe because of the general euphoria among the subjects, particularly as the experiment progressed, or during the test situation, or more so, when they felt they were being watched. For instance, an outsider viewing the men for the first time during the 4th day would not be able to detect differences in their behavior and activity from that of fresh, rested men. The fact that the subjects were always ready to respond to the presence of strangers by showing off contributed to this difficulty. A good example is an incident involving a group of 40 men on the 100th hour who were returning from a 10 mile march. The work program for this particular experiment was unusually heavy, the men looked fatigued and dejected and their clothes added nothing to their appearance. They approached camp via the parade grounds just as a battalion was marching in review. The lieutenant halted his group and addressed them, "Let's show them how real marines march." They did, for the next 15 minutes. Although this was undoubtedly a very elegant demonstration as to what "real marines" can do, it is an equally excellent example of the well-known difficulties encountered in studies designed to measure the effects of various conditions on performance. On the other hand, when the subjects were followed daily there appeared symptoms of the emotional type which resembled, in a degree, affective reactions such as: euphoria, followed by mild depressions; the dejected postures of the men when permitted to rest, or their restless pacing about; the indication of slowing down of mental activity; the apparent indifference to unusual behavior other subjects in the group showed, such as silly laughter, hallucinations, as well as the other disturbances described below.

A constant source of concern, particularly beginning the second night, was men straying off the line of march, walking into ob-

stacles, or falling (due to walking up or down steps or curbs that did not exist). Innumerable times men would walk into walls or bushes apparently with their eyes open. (Yet, during the test situation, no significant changes were found in visual acuity, depth perception, distance judgment and other tests of vision[6] although there occurred some increase in body sway.) Frequently, on sitting, they would unintentionally assume very uncomfortable positions and hold these positions while carrying on a conversation until it was called to their attention. These postural abnormalities and signs of incoordination occurred in waves interspersed by periods of apparently normal behavior.

3. Paranoid Reactions

In a number of subjects reactions occurred resembling acute schizophrenia of the paranoid type, such as delusions of grandeur, persecution, hallucinations and unprovoked aggressiveness with intent to do bodily harm.

The first incident occurred in an experiment with 35 men. Just before dawn of the 3rd day (after about 46 hours), the subject in question started walking off the line of march. He was brought into line and shortly started talking to himself. He became extremely aggressive and started an unprovoked fight with the man marching in front of him. From his conversation, it appeared he had delusions of grandeur. He insisted that he was in the Corps carrying out a secret mission for the President. He also claimed he was a secret agent ferreting out spies and traitors. He rambled on incoherently for a short while, then again became aggressive and unmanageable. He broke ranks and ran across a field and stumbled into a ditch. Two men were dispatched after him and he had to be forcibly taken to the dispensary and put to bed. He fell asleep shortly and, without any sedation, slept through the entire day and most of the next night. On awakening, he had no recollection of the events of the previous night, and when they were described to him, appeared ashamed and wept, concerned that he had "let his Company down." There was no indication of a predisposition in the history of this 19 year old to any abnormal behavior. He was generally well liked and was considered quiet and reserved.

A second incident occurred approximately at 2:00 a.m. of the second night of an experiment involving 60 men. The men were washing after having completed a march. One 20 year old volunteer started to cry hysterically. His conversation indicated delusions of persecution: he believed that the men in the room were trying to do him bodily harm because they were jealous of him. He became aggressive and suspicious. He was taken to the dispensary, given pentobarbital (1.5 grains) and put to bed. He slept until about 5:00 p.m. Examination, following breakfast, revealed that he had only very vague recollections of the events in the washroom, and he appeared genuinely surprised when told of his behavior. In this, as in the other cases, there was no history that could account for this reaction.

The third incident occurred in the same experiment and shortly after the washroom affair. This 18 year old subject was upset apparently by the occurrence in the washroom. He was already showing signs of increased irritation and became very profane. Without provocation he started a fight with an officer, also on the experiment, insisting he was being forced to continue against his will. (Up to this time, six men had dropped out of the experiment of their own volition.) He was taken to the dispensary and put to bed. He refused to take pentobarbital but within an hour fell asleep. He slept soundly for about 12 to 14 hours. On awakening, he vaguely remembered some, but not all, of the events of the evening. He appeared ashamed of the fight with the officer, whom he liked very much, and went quickly to apologize and try to rejoin the group. The lieutenant in question was his platoon leader who, incidentally, enjoyed the high regard of his men. He completely disregarded the incident, attributing the man's conduct to extreme fatigue. It was his opinion that normally the man was a good soldier.

The four cases of persistent auditory and visual hallucinations mentioned above were also accompanied by marked irritability and uncooperativeness. Their suspicious behavior, when questioned, their emphatic insistence that they *were* seeing or hearing real persons or sounds appeared to indicate true hallucinations. They were dropped from the experiment and put to bed. These subjects, on awakening, had little recollection of the events that had caused them to be dropped from the experiment.

Of the seven incidents mentioned above, only one subject was receiving medication other than a placebo, but because of the small number of cases this fact is without significance. This individual was in a subgroup receiving the thiobarbiturate. His complaint was that he insisted he was hearing and seeing a dog and he was certain the observer "was deaf, as well as blind and dumb!"

All signs and symptoms of the disturbances reported above disappeared after sleep. The great majority who finished the experi-

ments had only hazy recollections of events that had occurred during the previous 100 hours. Interestingly enough, certain psychomotor performance tests made on the men after a night's sleep showed changes over the last test that could only be attributed to learning.[6] This would appear to indicate that the learning process, at least that measured by reaction time tests, was not completely interfered with during sleeplessness. The individuals who exhibited the more bizarre disturbances were, for the most part, only embarrassed when they were informed of their behavior. There were no indications of residual personality or psychological aberrations. It was unfortunate, however, that the conditions of the experiment and the situation at the time made adequate follow-up impossible. It was more unfortunate that a complete personality background on the subjects was unavailable at the time of these experiments.

Discussion

The mild, transitory, wave-like psychological disturbances that generally result from sleeplessness, such as the increased irritability, the tendency to hallucinations, the disturbances in thinking, the apathy and catatonic-like behavior, taken by themselves, have no significance other than confirmation of observations of the behavior of otherwise normal men who are extremely sleepy.[1,3] Even the autistic expressions that frequently occurred could be attributed to dreams possibly occurring in this semi-sleep state. However, what lends significance to the occurrence of these mild symptoms is that in a significant number of cases the same symptoms, but greatly aggravated, occurred such as, true hallucinations and delusions instead of pseudo; unprovoked aggression and combativeness instead of irritability and uncooperativeness; completely irrational conversation with no insight instead of transitory periods of signs that indicated disturbed thinking. That these severe reactions in otherwise normal men were noted here for the first time is undoubtedly due to the use of larger numbers of subjects. It was the general impression that the differences in symptoms among all subjects on these experiments were principally those of degree.

It is also of some significance that behavioral aberrations first become apparent at approximately the time changes in the electrical activity of the brain occur.[7]

One can only speculate why some of these individuals responded to sleep deprivation with relatively severe disturbances. It is tempting to propose that a "latent" psychosis was prematurely induced by experimental insomnia. There is, however, little evidence to support this. It was pointed out above that little was known of the previous histories of the subjects used in these experiments, particularly their personality or psychiatric background, other than that all of them went through the general psychiatric screening given to enlisted men and volunteers during World War II. Furthermore, questioning, after a night's sleep, revealed little helpful information on those who exhibited the more bizarre reactions. Therefore, it cannot be stated whether or not the kind of reactions to sleeplessness shown in the individual cases were related to their "premorbid personality." *A priori,* it might be expected that were a latent mental disorder uncovered, the signs should persist longer than they lasted in these subjects. The psychotic reactions resulting from sleeplessness disappeared following a good sound sleep. It is our impression that latent mental disorders were not precipitated in the cases reported here. However, we do not intend to imply that sleep deprivation, like other forms of stress, cannot uncover such diseased states.

The rapid disappearance of these symptoms after a sound sleep resembles the state found in the toxic type of psychosis, particularly those reactions coincident to certain illnesses or overdosages of drugs. In such cases, the mental symptoms subside as the patient recovers from his illness or as the drug is eliminated. The symptoms shown by sleepless men are also similar to the reactions following brain injury,[9] particularly since there are associated with both types an abnormal electroencephalogram.[7,9] The toxic-like character of the reactions resulting from sleeplessness and the fact that all men participating in these studies developed such symptoms, in varying degrees, suggest the possibility of the elaboration (or depletion)

of some substance during prolonged wakefulness. Such a possibility brings to mind Piéron's[4] experiments which suggested that the brain of an animal kept awake for prolonged periods accumulated a substance which he called "hypnotoxin." This agent, he claimed, could be extracted from the brain or cerebrospinal fluid and, when injected into the 4th ventricle of another dog, caused not only marked drowsiness but brain changes characteristic of prolonged wakefulness. The exploration of this possibility is, for the time being, the basis of other studies from this laboratory.

For the present, the only conclusion warranted by the findings of these studies is that the deprivation of sleep produces a disturbance of an unknown nature in the functioning of certain areas of the central nervous system. As a result, behavioral symptoms occur that have some of the characteristics of certain psychotic disorders encountered clinically.

Summary

1. After approximately 40 hours of sleep deprivation there occurs in all subjects psychotic-like reactions. In the great majority of subjects the symptoms are mild; in some the reactions are severe, resembling acute schizophrenia of the paranoid type.

2. In all subjects, the symptoms disappear following sleep.

3. The significance of the resemblance between the psychic reactions resulting from sleeplessness with those occurring in toxic psychosis is discussed.

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Meratran

Preliminary Report of a New Drug for the Treatment of Behavior Disorders in Children

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The medical treatment of the behavior disorders of childhood is once more reverting in part to pre-Freudian concepts, after a generation of treatment consisting primarily of psychiatric and psychological approaches. This is also true of the treatment of adults, as can be attested by the voluminous literature relating to chlorpromazine and the rauwolfia derivatives. Interest in the medical treatment of behavior disorders does not mean that we are ignoring the vast experience obtained from the psychiatric approach, but rather that we are again beginning to consider the individual as a unit, instead of an empyreal ego with no relation to the brain or to the body. The "brain is the organ of the mind"[1] and to consider behavior without considering possible abnormal physiology is to overlook basic considerations.

Laufer, Denhoff, and Rubin[2] have shown that in the hyperkinetic syndrome of behavior there is a lowered Metrazol-photic threshold, and that this lowering can be overcome by the use of amphetamine sulfate. This finding fits in well with the observations of Bradley[3] and of Walker and Kirkpatrick,[4] that behavioral disorders can be aided by various types of anticonvulsants, such as the amphetamines and Dilantin. The fact that anticonvulsant drugs are not primarily sed-

atives but range over a broad field of chemicals which seem to be particularly related to various enzyme systems is also well demonstrated in this study. Thus, we find amphetamines which act as amine dehydrogenase inhibitors,[5] succinimides such as Milontin which activate the tricarboxylic acid cycles,[6] barbiturates which inhibit choline esterase,[7] Diamox which is a carbonic anhydrase inhibitor,[8] and others.

If it seems unusual to bring the anticonvulsants into a discussion of behavior, attention may be called to the fact that all of the drugs mentioned, or their related substances, are known to have a profound effect upon behavior. The succinimides which probably seem the most unrelated are included, since di-isopropyl fluorophosphate, which inactivates choline esterase and produces profound psychotic or pseudopsychotic reactions in behavior,[9] has these reactions reversed by succinimides.

The addition of each new drug for the treatment or control of behavior moves us a step further. The interest in various drugs waxes and wanes. Thus calcium and thyroid, which in their day were hailed as "the answer," have sunk back into their small but useful roles and are used only occasionally for the control of behavior disorders.

Each new drug must thus be evaluated critically, and few indeed are those which have been used for the treatment of behavior disorders for more than ten years.

Meratran (α-(2-piperidyl) benzhydrol hydrochloride) is a new antidepressant drug which has recently been reported to be of help in a number of disturbed states. Brown and Werner[10] first reported the pharmacologic actions of this drug, which led Fabing to try it in narcolepsy[11] and in tics,[12] while Andren used it in 17 patients with depressed states.[13] In all of these, good results were reported. Schut and Himwich[14] evaluated Meratran in 25 institutionalized mental patients, and found it to be of value in schizophrenics without delusions, in psychomotor retardation, and in deteriorated schizophrenics. Pomeranze[15] found that it increased alertness and *joie de vie* in the geriatric patient. Antos[16] showed that it elevated mood without producing anorexia and the "hopped-up feeling" often associated with amphetamine therapy. Meratran has also been found to be a useful adjunct in the dietary treatment of obesity,[17] which in view of the lack of anorexia reported in other studies, would indicate that the action of the drug was related to improving the emotional status of the patient rather than to a direct anorexic effect.

Present Study

In view of the above reports, Meratran was tried in 47 patients, who were distributed in sex and age as shown below:

SEX:

Male 35						Female 12					
Age	5	6	7	8	9	10	11	12	13	14	15
Number	3	3	2	8	4	8	4	5	6	1	3

For the present study, no attempt was made to classify completely the type of behavior disturbance. The criteria for diagnosis were simply that the child was unable to live at peace with his environment, peers or family, and that this was the observation of more than one individual; or that in the presence of normal intellectual ability as measured by the WISC, Stanford Binet and Goodenough tests, the child was doing poorly or failing work in school. Psychological evaluations were done in most of these children, but definitive correlation seems impossible because of the few numbers involved. No frank psychotics were included.

Epileptics were considered primarily because of associated behavior disorders or lack of control with other drugs.

All observations were for periods of more than three months, except in those cases that were made worse.

Methods

The patients used in this preliminary study were selected without differentiation between those in whom organic factors could be related definitely to changes in function or emotional stability and those in whom the prime factor seemed to be environmental. Since a preliminary division into organic and emotional would have introduced one possible source of error, it was decided to go on the basis that a more definitive answer could be obtained by taking all patients as they came. With a larger series, more attention to complete classification would be of value.

No extra counciling or psychotherapy was used during the course of therapy, but it must be borne in mind that simply telling the children and their families that this drug would help constituted some counciling.

All patients had Bender Gestalts and Good-enough Draw-A-Man tests done before beginning the medication and at each visit, and these have been evaluated for degree of improvement.

Electroencephalograms were done on 40 of the 47 patients. These were all done on an Offner 8 Channel Model D, using bi-polar technique. Interpretations were done by Dr. H. Sjaardema and the author. The borderline classification includes those on which there was disagreement as to interpretation. Hyperventilation was used in all patients for activation. No follow-up electroencephalograms have been done.

Improvement or lack of it was judged on the basis of reports from the family, school, personal observation and changes in performance on testing. Results were classified as follows: no change, fair, good, excellent, worse.

Meratran dosages varied from 0.5 mg. to 3.0 mg. daily. All children under ten years of age were started on 0.5 mg. daily; all over ten, on 1.0 mg. daily. All patients required greater than 1.0 mg. daily for best control.

The over-all results of treatment may be seen in Table I.

TABLE I

Results:	*No change*	*Fair*	*Good*	*Excellent*	*Worse*
Number	12	3	10	12	10

These results showed that there was some degree of improvement in behavior in about fifty-five per cent of cases (25 of 47). Approximately twenty per cent (10 of 47) were made worse, and twenty-five per cent (12 of 47) showed no change. Only one of the ten epileptic patients showed any change in the status of his epilepsy, but since such a small number was included no conclusions can be drawn.

TABLE II

Results in Relation to EEG Findings

TYPE OF EEG	RESULTS				
	No change	*Fair*	*Good*	*Excellent*	*Worse*
Normal	2	1	1	1	1
Abnormal	9	2	4	7	6
Borderline	1	0	2	1	2
No EEG	0	0	3	3	1
Totals	12	3	10	12	10

Results of treatment were then correlated to the type of electroencephalogram found, and the correlation is shown in Table II.

From Table II it can be seen that the results of treatment could not be predicted on the basis of the electroencephalographic findings. The results were approximately the same in those patients having abnormal electroencephalograms as in those having normal electroencephalograms. This finding is not too unexpected, since it has been commonly observed that in those patients having epilepsy and a normal electroencephalogram results were similar to those obtained in patients with epilepsy and an abnormal electroencephalogram.

Five of the 12 patients whose progress was classified as excellent were children who in spite of an over-all normal intelligence as measured by the WISC or Stanford Binet were doing very badly in school. In these five, several of the teachers noted improvement and commented that such overnight changes were unbelievable or remarkable, and they checked with the parents to see if they had any explanation for the change.

Results were usually seen within one week and always within two.

In those children who were made worse, there was an increase in irritability, a further loss of concentration, and several became "mean." These symptoms disappeared within three or four days after stopping the Meratran.

Blood counts, urines and urine urobilinogens showed no abnormalities in any of the patients studied, although these tests were done regularly.

Discussion

The over-all results obtained with Meratran in the treatment of children with behavior disorders are not quite as good as those reported for amphetamine,[3] but compare well with those reported for chlorpromazine,[18] Reserpine[19] and Diamox.[20] It has an advantage in causing no major toxic side effects, such as have been described for chlorpromazine. It has a real advantage over the amphetamines in that it does not habitually produce anorexia or insomnia. Many of our patients, in fact, showed better

sleeping and eating habits when taking the medication than they had before taking it. Meratran can be given in the morning, or twice daily, morning and evening; this is important in chilrren, since a noon dose is a major hurdle to a child of school age.

The site of action of this drug, according to Fabing,[21] is in or around the hypothalamus, and our own results would seem to indicate that its action lies in increasing the attention span and decreasing irritability, with a resultant increase in function. These actions may be mediated through the arousal system of Magoun.[22] It would be of great interest to determine which of the enzyme systems are affected by this drug.

Conclusions and Summary

1. Meratran produced improvement in the behavior of 27 of 47 patients diagnosed as behavior disorders of childhood.
2. Ten of the 47 were made worse by the medication, but in all cases this untoward result was reversible.
3. No major toxicities involving the liver, hematopoietic system or kidneys were found.
4. There was no correlation between the electroencephalographic findings and the results obtained.

Dilantin is the trade-mark of Parke, Davis and Company for their brand of diphenylhydantoin.

Milontin is the trade-mark of Parke, Davis and Company for its brand of methylphenyl succinimide.

Diamox is the trade-mark of Lederle Laboratories Division of American Cyanamid Company for its brand of acetozoleamide.

Meratran is the trade-mark of The Wm. S. Merrell Company for its brand of pipradrol. The Meratran in this study was supplied through the courtesy of Raymond C. Pogge, M.D., Director of Medical Research.

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Monopolar Electro-Shock Therapy

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Since the introduction of electro-convulsive shock therapy, constant research has been directed towards two goals. First, to find how or why it is effective; and second, to refine it so that it will retain, or even increase, its therapeutic efficacy and simultaneously be freed from its hazards. A number of explanations have been offered to account for the remedial effects of electro-shock. It is highly doubtful whether the convulsion per se is the basis for the therapeutic result. What is more likely is that, in association with the violent explosive state of the nervous system, there are liberated certain substances or hormones which play a part in the recovery of the individual. We know, for example, that the autonomic nervous system is profoundly stimulated in the process. There is considerable evidence that there are increased adrenocortical activity and alterations in chemical balance of the nervous system. We must not lose sight of the fact that improvement in many mental illnesses can be attained by non-convulsive methods such as psychosurgery and insulin coma; most recently drugs of the chlorpromazine and reserpine group have also shown promise. We must also bear in mind that metrazol-induced convulsions are therapeutically as effective as electrically induced convulsions. The electrical stimulant as a convulsive agent has largely replaced metrazol because of its obvious superiority. It is induced in a simpler manner and causes less anxiety in the patient and fewer complications, especially less damage to the peripheral vascular system.

Electric convulsive therapy, as it was first introduced, followed the technique of Bini-Cerletti and was administered by a 60 cycle AC type of current. The hazards and complications of this method are too well known to require elaboration, except to divide them into two main classes, namely, physical and psychological. The most severe physical complication is, of course, death due to cardiac failure. Others include respiratory failure so severe as to require artificial respiration, fractures of long bones or of the pelvis, and spinal compression fractures, as well as severe disabling pains in the back, chest, or shoulders.

Psychological complications consist in confusion, amnesia, loss of word choice, and forgetfulness, which at times is present to a frightening degree, causing humiliation and embarrassment to the patient. They may see strangers and think they have met them before; they see acquaintances and forget their names. Friends talking to them, refer to an incident of the day before, and the patient will deny that he was present or even that the incident occurred at all. School teachers forget the names of their pupils; physicians forget what their patients have told them.

It is in quest of methods to overcome these difficulties that modifications of the conventional type of electro-shock therapy have been sought. This paper will confine itself to the description of a new technique in the administration of the electric current which offers promise of greatly reducing, if not entirely removing, the hazards and complications of electro-shock treatment, although retaining its therapeutic efficacy. It consists of a unipolar or monopolar application of the current to one or several selected areas of the intact skull. The direction of the current from the monopolar zone of application is sagittal and deeply penetrative, in contrast to the transcortical direction between bipolar electrodes. The rationale for this method of treatment originated with the premise that the conventional method of inducing a convulsion was associated with unnecessary and uncontrolled violence in the administration of the electric current with resultant undesirable consequences. As we know, the AC current dosage or voltage is empirically pre-set, and it is literally shot into the skull by a trigger or push button mechanism. The moment the treatment lever

From Pinewood Sanitarium, Katonah, N. Y.
Read at the meeting of the American Psychiatric Assn., Atlantic City, N. J., May 9, 1955.

is depressed, there is no possibility of altering or diminishing the current. There is an instantaneous violent convulsive state, and the administering physician sits back in anxious prayerful apnoeic anticipation, hoping he will hear no bones cracking, and holding his breath until the patient sounds the first respiratory note.

With the advent of the unidirectional low voltage type of current, the intensity and amount of current is brought under the doctor's control and convulsions may be more gradually induced.[1] The convulsive threshold can be easily ascertained, and complications, both physical and psychological, therefore, diminished. The fact that the low intensity unidirectional currents apparently produce fewer complications, is most likely due to their being introduced gradually to the convulsive threshold.

Both the AC technique of ECT and the unidirectional low intensity currents introduce the currents in a similar manner through the skull by bipolar placement of electrodes generally bitemporally or bifrontally. The current courses through both cerebral hemipheres from pole to pole, only diffusely reaching the deeper structures, which there is reason to believe, play an important role in the autonomic and emotional balance of the body. It is believed that the bipolar method, although accomplishing its aim by producing a convulsion, does it by a non-specific overwhelming diffuseness of stimulation. It was postulated that there are specific "trigger zones" which, if stimulated, should produce an immediate convulsion. Assuming that such zones are located successfully, and current applied, it would logically follow that the ensuing convulsion would be produced by an amount of current below the minimum level hitherto considered necessary to produce a convulsion by the bipolar methods. It was also believed that other zones could be selectively stimulated so that currents would penetrate and pass through them.

The monopolar or unipolar method to be described was devised in an effort to accomplish this through altering the direction of the current in the brain as necessary. This is done by applying a single active electrode to certain areas of the skull and conducting the current through the medulla and brain stem in a line to the point of application of the monopolar electrode. Thus, if we consider the brain a mass of gel and assume that there is a fixed point of entry of the current, then the direction it will take will vary with the point of application of the active monopolar electrode to the head. The fixed point of entry is most likely the foramen magnum, to which the current is conducted by means of the indifferent cuff-shaped electrode applied to the right forearm. By altering the position of the monopolar electrode, one can pre-select the anatomical structures which it is desired to stimulate. In this manner, the various nuclei of the optic thalamus or other deep structures can be stimulated by proper placement of the electrode. The current, in this way, passes in a modified sagittal direction penetrating selected zones, including the reticular activating substances from the medulla on up through the cortex.[2] Thus, by conducting the current through the region of the vertex, the motor strip is stimulated, along with the thalamic nuclei, and a convulsion is rapidly induced with very small amounts of current. Placing the electrodes more frontally produces a greater stimulating subconvulsive effect and affects the frontothalamic pathways.

Evidence of the deeply penetrative quality and profound effect of this type of stimulation has been discussed in a previous paper which described the non-convulsive techniques in connection with the monopolar introduction of the current.[3] In brief, it should be pointed out that when the current is introduced to one side of the skull, whether it be frontally, temporally, or parietally, instantaneous bilateral clonic movements appear with currents as low as 3 ma. This is in spectacular contrast to the reaction to bipolar electrodes placed laterally on one side of the skull, when convulsive movements appear on the contralateral side of the body. The appearance of bilateral convulsive movements upon monopolar stimulation can only be explained on the basis of the action of the current in being conducted sagittally through the brain. The effect is either produced by biateral stimulation of the pyra-

midal tracts in the medulla and brain stem or by stimulation of convulsive centers in the thalamic or subthalamic regions.[4]

Monopolar Subconvulsive Technique

The patient lies flat on his back with arms folded over his chest. He is anesthetized with 5 per cent Sodium Pentothal given intravenously. Anesthesia is necessary in subconvulsive stimulation because the current at low intensity is painful and in fact has an awakening effect within 1-3 minutes after stimulation is started. An indifferent, cuff-shaped, electrode is applied to the right forearm.* Before application, both electrodes are thoroughly wet in an electrolytic solution, such as very dilute saline or soda bicarbonate. The active electrode consists of a disc about the size of a nickel piece attached at the bottom of a small insulated handle. The treatment is administered by applying the active electrode over the areas where stimulation is desired. By virtue of the unipolarity of the current, the physician can make or break the circuit manually, by merely lifting it from the head, and thus can change the area of stimulation at will.

In the subconvulsive stimulation three areas on each side of the head are subjected to the unipolar stimulation for ten second each. The amount of current required is generally 4-5 ma. This induces profound stimulation of the autonomic nervous system, and bilateral convulsive movements of the extremities. The first electrode position is in the midpupillary line above the orbital ridge; the second portion stimulated is at the hair-line in the midline; the third is in the temporal region just in front of the ear. Treatment is generally given bilaterally, making a total of six areas stimulated. While the current is on, the patient is in a convulsive state. The moment the current is turned off, he resumes breathing. He is generally allowed to rest for five to ten seconds between each stimulation to re-establish good respiration. Thus, the total time of current application is about 60 seconds and the total duration of the treatment is about two minutes.

Monopolar Convulsive Technique

The preliminary preparation of the patient is the same as in the non-convulsive method, except that here it is not necessary to anesthetize the patient, since a total convulsion and comatose state is rapidly induced. If the patient should have anxiety or fear of treatment, he may be given intravenous sodium pentothal or sodium amytal in a subanesthetic dose—just enough to produce relaxation and calmness. The cuff electrode is applied as described above. The active electrode may be applied in a sagittal plane at a point about 3 cms. in front of the vertex of the skull or to any spot 2-3 cms. lateral to the midline. The midpoint is approximately at the spot where a sagittal line crosses a line between the tips of the ears. By applying the electrode within a space up to 2 cms. lateral to the midline, the current can be made to pass up through the medulla, pons, reticular activating substance, and the various thalamic nuclei. The placement of the monopolar electrode is thus over or near the motor strip of the cortex.

Using the Reiter Apparatus (RC 47C) and the current selection knob at position 5, with high modulation, a convulsion is induced within two to five seconds with 15 ma. of current. The convulsion is ushered in with a tonic phase which soon becomes clonic. The jerkiness of the latter is easily controlled and the convulsion retains a smooth quality by the doctor's maintaining the current at about 5 ma. for thirty to forty seconds, and then turning the current off, at which time the convulsion physiologically is about to terminate and the respiration returns.

It is possible to induce a convulsion with 7 to 10 ma. of current, but in some instances, the patients have reported that they were aware of the treatment, and described it in various ways. This, in spite of the fact that a classical grand mal convulsion was induced, as evidenced by its continuation for thirty to forty-five seconds with the current off and with complete apnea during the period. Some of these patients, just before awakening, exhibit a tendency to noisy hypernea for one or two minutes; the type of breathing being similar to that seen in one resting after physical exertion from running.

*Electrodes supplied by Reuben Reiter, ScD.

This reaction is entirely avoided by starting the initial stimulation at 15 ma.

Combined Monopolar Convulsions And Subconvulsive Technique

In this method a convulsion is induced as described above. As soon as breathing commences and during the minute or more when the comatose state remains, it is possible to change the position of the positive electrode and apply it to the areas described above under subconvulsive stimulation. In this way, the patient is not only given the benefit of general convulsive therapy, but there is additional stimulation of areas of the frontal lobe and adjacent areas corresponding to the zones involved in lobotomies.

Discussion

The monopolar method of electro-cerebral treatment introduces a technique of applying a deeply penetrative current. Its direction is approximately sagittal and its action depends on its passing through the medulla and brain stem and stimulating the reticular activating substance while affecting various of the thalamic nuclei and other subcortical structures in its path. The monopolar treatment requires a fraction of the current necessary in any of the other methods. An average current of 10-15 ma. for a duration of three to four seconds usually suffices to induce a convulsion. It should be made clear here that by a convulsion, we mean a bilateral paroxysm of the entire musculature, either tonic, clonic, or both, having decerebrate components and associated with apnea throughout the length of the convulsion. This condition lasts from thirty to forty-five seconds, irrespective of the duration of the initial stimulus which induced the convulsion. A sub-convulsive movement, on the other hand, is one which spontaneously ends at the instant the stimulus ceases, at which point breathing resumes. Thus, with the monopolar method of introducing currents sagittally through the brain, we are able to induce convulsions or subconvulsive movements, depending on the selection of the site for application of the active electrode and the amount of current used. It should be emphasized here that all subconvulsive movements as well as convulsions, which are induced by this method are *bilateral,* commencing with average currents of 3-5 ma. This is particularly noteworthy when one realizes that in the monopolar technique of stimulation, the current passes through only one cortex (not considering the effects of 'spread' with larger currents), and it would therefore be expected that contralateral movements would ensue at once. *But this is not the case.* To explain the bilateral response with unilateral stimulation, one must either postulate that as the current passes through the medulla or brain stem it stimulates the motor pathways bilaterally, or, that there are certain convulsive trigger zones in the thalamus or elsewhere, which are set off by the passage of the current.

The fact that convulsions are easily induced and with such minimal currents, has self-evident advantages. Certainly the danger of damage to cerebral tissue is practically eliminated. One very definite finding in relation to this type of treatment is that it eliminates psychological complications. In none of our cases was there confusion, forgetfulness, or any other type of memory disturbance noticeable as a residual of the treatment. This may be due to the sagittal direction of the stimulation, which means that there is less disturbance of the cortex than in the transcortical or horizontal path of the current with the bipolar method of treatment. The tremendous advantage of being able to treat patients with the assurance that they can carry on their daily work with normal command of their memory needs no further comment. The hazard of complications due to fractures is also greatly reduced. The monopolar induced convulsion lacks the violent explosive tetanic quality of other methods, which often is responsible for bone injuries. The clonic movements associated with the convulsion of the monopolar current are quite vigorous, but are easily controlled, (as is possible with low amperage unidirectional currents) by maintaining a small amount of stimulation—5 ma., for the duration of the seizure. Another advantage is that the patient isn't as anxious and fretful when an electrode is applied to his forearm as when a headband and electrodes are placed around his head. The active monopolar electrode is manually applied just as

treatment begins and the patient therefore has no memory of electrodes applied to his head. New research possibilities are obviously presented by this method, since specific structures can be selected for stimulation. By placing the active electrode from 5 to 25 mms. lateral to the midline, the current can be passed with reasonable certainty through specific structures, such as the formatio reticularis, the globus pallidus, the red nucleus, and the various nuclei of the thalamus. It should be possible with non-convulsive amounts of current to stimulate the deeper structures of the brain and to learn whether the same changes in cerebral metabolism, hormone production, etc., which have been demonstrated by inducing convulsion, might not also be produced by directly stimulating specific deeper structures without inducing a convulsion.

The clinical results obtained with the monopolar method apparently parallel that obtained by the other electro-shock methods. In our clinic, we have treated over 100 unselected cases with this method. The patients received over 1200 treatments, averaging 12 treatments each. We have over 80% recoveries in the manic depressive and involutional group of psychoses. A number of recurrent manic depressives were treated with this method. In these cases, we knew how many convulsive treatments had previously brought about recovery from their psychoses. These cases had previously received the conventional AC method or the unidirectional low intensity currents. We found that an equivalent number of convulsions induced with the unipolar method, brought about recovery in these cases.

In our original work, we used subconvulsive stimulation applied to various frontal areas exclusively. This method lends itself particularly to treating patients whose physical conditions make convulsive treatment too great a risk. We felt that the non-convulsive method was effective in many cases but was not as efficient as the convulsive method. We also noticed that by "topping off" the non-convulsive treatments toward the end of a series with one or two convulsions, sudden dramatic recovery frequently ensued in patients who were much improved, but not entirely well. With this experience in mind, and in view of the simplicity of producing convulsions, we modified our approach in therapy and have been giving monopolar convulsive treatments to patients whenever possible—particularly to depressives and involutionals. Schizophrenics, psychoneurotics, and others for whom the prognosis is not so favorable, are given the combined treatment. This consists in first inducing a convulsion and utilizing the minute or two after the termination of the seizure, and while the patient is still comatose, to apply frontal subconvulsive stimulations described above. We have had many social recoveries in schizophrenics through this combined method of treatment. Before any definite conclusions can be drawn, however, many more cases will have to be treated and parallel studies made to determine the statistical differences in results between patients treated exclusively with convulsions and those treated with the combined method.

Summary

Electro-cerebral stimulation which induces convulsions is at present a method of choice in treating certain types of mental disease. Physical and psychological complications, which have constituted an obstacle to the treatment, have stimulated workers to alter or modify the original types of current used, or their technique of application. The common purpose is to make the treatment less dangerous while retaining its stimulative or convulsive efficacy. The basic hypothesis of the monopolar method of treatment is that certain specific areas of the brain may be the "trigger" zones which require stimulation to set off the convulsion or other therapeutic reactions. By introducing the current through a monopolar electrode, there is deeply penetrative directional selection obtained. Desired results ensue with fractions of the amounts of current used in bipolar methods. There is therefore a corresponding diminution in the harmful or destructive side effects frequently encountered by the conventional methods. In contrast, present bipolar methods of treatment introduce the current bifrontally or bitemporally and in association with the production of the convulsion diffusely stimulate cortical and subcortical structures. It is believed that these

excessive amounts of current and uncontrolled diffuse stimulation may be responsible for unwanted complications occurring in connection with the bipolar method of electro-shock therapy. With the monopolar method, we can produce stimulation or convulsions, depending on the zone of application of the active monopolar electrode. As a result of the "aiming" of this current at specific locations, average treatment values of 5-15 ma. are sufficient to produce a desired reaction. So, being able to accomplish therapeutic effects with such minimal currents, the danger of cerebral pathological changes is eliminated. The convulsion can be ushered in slowly under the control of the physician, and is less violent than with other methods and thus the hazard of bone injuries is minimized. Further, by virtue of the sagittal direction of the current, (sparing excessive stimulation of the cortex), memory changes such as confusion or forgetfulness are avoided. All these benefits ensue while the clinical results parallel those obtained with any of the other methods of electro-convulsive treatment now in use.

The current utilized by the monopolar treatment is a low intensity, unidirectional pulsating spiked wave, (Reiter RC47C apparatus). It is led out through a monopolar electrode (negative pole) which is manually applied at the base of an insulated handle over selected areas of the intact skull. An indifferent electrode (positive pole) is attached as a bracelet to the right forearm. The current thus enters the medulla through the foramen magnum and extends in a sagittal direction, making its exit at the point of application of the monopolar electrode. Electrodes may be held over various frontal areas, or on either side of the midline near the vertex, depending on the structures which one wishes the current to pass through. It is deeply penetrative and can thus be conducted through various sagittal sections of the brain, stimulating the reticular activating substance and the thalamic nuclei. This technique offers new possibilities in neurophysiological research and psychiatric therapy.

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ERRATUM

The editors regret the occurrence of an error in printing in the article "Technique for the Modification of Electroshock With Succinylcholine" by Dr. H. Jerome Rietman and Dr. Enrique Delgado published in the August 1955 issue of DISEASES OF THE NERVOUS SYSTEM. At the bottom of page 237, a line was inadvertently omitted. The last sentence on the page should read "Approximately 20 milligrams of succinylcholine per 50 pounds of body weight is injected."

NOTICE OF MEETING

The Thirty-Fifth Annual Meeting of the Association for Research in Nervous and Mental Disease will be held on December 9th and 10th, 1955 at the Hotel Roosevelt, New York City. The subject of the meeting will be "The Neurologic and Psychiatric Aspects of the Disorders of Aging."

The Protein Profile In Chlorpromazine Therapy

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With the recent introduction of chlorpromazine as a therapeutic agent in neuropsychiatric and allied disorders, there have been an increasing number of articles with empirical information on the clinical changes and the toxic manifestation of this agent.[1,7,15,16]

The purpose of this paper is to make a preliminary report on a definite biophysical change noted to be associated with the administration of chlorpromazine. We were first directed toward the problem of detecting some physiological change by the observation that Wilson's Syndrome (hepatolenticular degeneration) was clinically similar to some of the toxic reactions of chlorpromazine. Working with this in mind, we attempted to discover some change either in the liver function or in the serum protein fractions.

Methods

Nine female schizophrenic patients, all on the same hospital ward, and all without any apparent physical disease, ranging from 28 to 70 years of age, were chosen for this study. Serum samples were obtained from each patient on three different days before chlorpromazine therapy. The patients were then given 100 mg. of chlorpromazine per day for a period of two weeks and then three additional serum samples were drawn at weekly intervals from each patient while they were still receiving the drug.

On both the pre-chlorpromazine serum samples and the samples taken during therapy a battery of liver function and hematological tests were performed. All samples of serum were separated into their protein components, using paper electrophoresis and dye elution techniques for quantitation.

The hanging strip paper electrophoretic cells used in this study were of lucite construction with platinum electrodes and built on the principle of the Durrum model.[2] The strips were of Whatman 3 MM filter paper, 3 cm. wide and 12 inches long. The standard veronal buffer of a pH 8.6 and ionic strength of 0.075 was used. The filter paper strips were first saturated with buffer and 0.01 ml. of serum was applied by means of a commercially available striper. All separations were run at 1.0 ma per strip from 16 to 20 hours at 4° C.

The strips were then removed from the cell and oven dried in a horizontal position for 30 minutes at 110° to 120° C.[2] After drying they were handled in the method outlined by Block, Durrum, and Zweig[2] which involves staining in a Bromphenol blue dye for 16 hours, followed by two five minute washings and one ten minute washing in 2% acetic acid and one two minute washing in a mixture of 2% sodium acetate and 10% acetic acid. The strips were then redried at 110° to 120° C. for twenty minutes.

The stained serum partition patterns were scanned using a photoelectric densitometer. The optical density of each protein fraction was plotted as the ordinate against the distance migrated as the abscissa. These plots constitute a graphic representation of the serum patterns. The points of least density between serum fractions were determined by superimposing the graphs on the stained strips. These points were used as a guide when the strips were cut for the fractional elution of the dye.

The dye was eluted from each section of filter paper with a 10 ml. aliquot of 0.01 normal NaOH. Good results were obtained in this laboratory by placing the tubes containing the NaOH and filter paper sections in a mechanical shaker for ten minutes during the elution. The paper sections were removed from the tubes and optical densities of the resulting solutions were measured within one hour on a photoelectric spectrophotometer at a wave length of 590 mu., using a light path of 19 mm.

Discussion

No significant change was found in the cephalin cholesterol flocculation, thymol turbidity, serum total protein, icterus index, or

From Research Center, Western State Hospital, Fort Steilacoom, Washington.

the hemogram of any of the nine patients before or during chlorpromazine therapy. However, a change was noted in the serum electrophorectic patterns of all of the patients studied. In seven out of the nine patients there was a slight decrease in the serum albumin fraction after the administration of chlorpromazine. Also in all the patients tested an increase in the beta globulin fraction was demonstrated (Table I). With this increase there appeared a beta globulin separation into two components, a so-called "Beta Split"[14] into a beta-one and beta-two fraction.

TABLE I

COMPARISON OF SERUM PROTEIN FRACTION

Averages Before and During Chlorpromazine Therapy

BEFORE CHLORPROMAZINE THERAPY

No.	Albumin	Alpha-1	Alpha-2	Beta Total	Gamma
1	50.29	6.02	9.99	9.72	23.88
2	56.20	5.10	9.20	12.90	16.60
3	52.90	6.63	12.38	10.90	16.77
4	45.40	5.10	9.90	13.60	26.00
5	58.11	5.39	9.86	10.83	15.85
6	52.90	4.90	11.20	8.90	22.00
7	53.00	5.50	11.20	10.90	19.60
8	46.50	6.70	14.50	12.10	20.10
9	37.51	6.72	13.39	9.08	33.27
Averages	50.31	5.78	11.29	10.99	21.45

DURING CHLORPROMAZINE THERAPY

No.	Albumin	Alpha-1	Alpha-2	Beta-1	Beta-2	Beta Total	Gamma
1	47.27	5.84	10.31	7.85	5.85	13.70	22.86
2	46.28	7.27	12.79	9.55	6.98	15.90	17.76
3	43.40	8.07	11.13	9.67	9.34	19.40	18.17
4	40.30	6.20	11.20	9.00	9.70	18.70	23.60
5	53.00	6.50	11.30	8.70	7.60	16.60	19.70
6	50.30	7.30	10.60	7.50	6.80	13.30	18.60
7	43.40	6.60	12.20	9.20	9.00	18.20	19.70
8	50.77	5.50	10.97	7.23	6.60	13.83	18.87
9	43.43	5.04	8.68	4.95	4.89	9.74	28.17
Averages	46.46	6.48	11.02	8.18	7.30	16.00	20.82

The average pre-chlorpromazine albumin fraction for the nine patients studied was 50.31% of the total protein. During treatment this fraction was found to be reduced to 46.46% of the total protein. The average pre-chlorpromazine beta globulin fraction for the nine patients was 10.99%. The average beta globulin fraction during therapy was increased to 16.00%. This represents an increase of approximately one-third in the beta globulin fraction over the pre-chlorpromazine level. The average alpha-one, alpha-two, and gamma globulin fractions during therapy were all within 0.7% of the pre-chlorpromazine averages. In the total protein, no significant change was found from pre-chlorpromazine levels.

The beta-two fraction which appeared after chlorpromazine therapy, but which was not demonstrated in the pre-chlorpromazine patients moves with an anodal migration, and has a somewhat slower migration rate than the normal beta globulin fraction, but a faster rate than the gamma globulin fraction as shown in Figure 1.

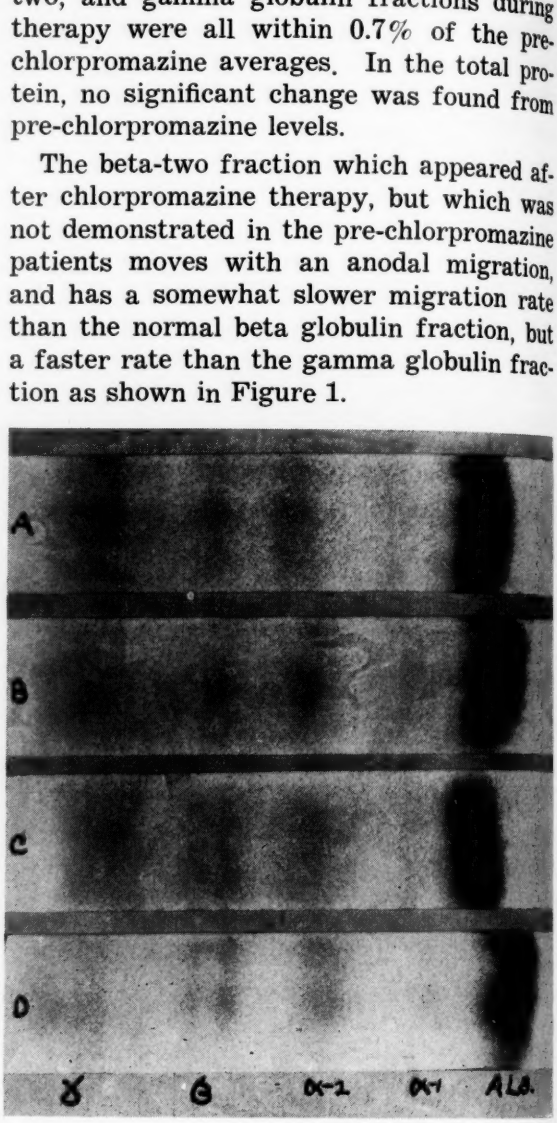

Figure 1. Electrophorectic Patterns of Pre-Chlorpromazine (A & B), During Theray (C & D) Demonstrating a Separation in the Beta Globulin Fraction.

The above data indicates that there appears to be a correlation between the protein fraction. The possibility that this beta split was due to a buffer artifact or to duration of run as reported elsewhere[8] was ruled out by simultaneously electrophoresing a normal control serum in the cell with the chlorpromazine sera.

It has been established that serum albumin is produced by the liver.[4] Therefore, un-

der certain conditions changes in the serum albumin fraction may be interpreted as a reflection of hepatic activity. White and Dougherty have shown that both beta and gamma globulins are increased in rabbits following the injection of either adrenotropic hormone or adrenal cortical steroids.[17] Serum beta globulins have been reported by various investigators to be increased in dogs[3] rats, and goats[5] injured with vesicants, heat[6] and turpentine.[13] Also, they are increased in some cases of virus hepatitis and liver cirrhosis.[12] Stern and Riener have considered an increased serum beta globulin as a manifestation of hepatic parenchymatous disorder evidenced microscopically by focal areas of necrosis, and my pyknosis of the liver cell nuclei. In liver cirrhosis the albumin is decreased and the beta and gamma globulins are increased.[14] Other investigators have reported finding two beta globulin fractions[10,11] or beta splitting[8] but, little reference was found correlating this phenomenon to any pathological entity. In a personal communication, Dr. Oosterhuis made the observation that this beta separation also occurs in cases of infective diseases, acute rheumatism, pregnancy and carcinoma metastasis.[9]

Summary and Conclusions

The quantative data on an electrophoretic study of nine female patients, before treatment, and also during treatment with chlorpromazine, has been presented. The results indicate that there is a slight decrease in the albumin fraction and a more pronounced increase in the beta globulin fraction in patients receiving the drug. Also, there is evidence that this increase in beta globulin is due to a separate beta fraction with a migration rate a little less than that of the normal pre-chlorpromazine beta globulins. The above preliminary studies indicate that there appears to be a correlation between the chemotherapeutic agent, chlorpromazine, and an increase in the serum beta globulin.

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Mental Disorders and Thyrotoxicosis

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The importance of psychological or psychophysiological factors in the development of thyrotoxicosis has been stressed by a number of workers, and this subject has been focused from different angles.[2,3,4,5,6] Alexander[1] has mentioned "the hyperthyroid patient is one who has been trying to maintain a lifelong struggle against his anxiety." The remarkable similitude between psychic states with overwhelming anxiety and the early phases of hyperthyroidism is also very well known. Tachycardia, palpitations, hyperexcitability, apprehension, emotionalism, changes in personality, cycloid and schizoid tendencies are found in most of the cases of toxic goiter.[8] The same symptoms can be found in different types of mental disorders, mainly in psychoneurosis, according to the degree of development and with the content of anxiety.

The purpose of the present article is to demonstrate that this anxiety with thyrotoxicosis is part of the onset of a determined mental disorder and if recognized in time, instead of thyroidectomy, the patient should receive active psychiatric treatments.

For the purpose of this study the following material was taken from the records of the Warren State Hospital, whose present census is 4583 patients (3195 in-residents and 1388 on leave-of-absence). Of these, 63 had had thyroidectomies performed before commitment. Nine cases were not considered because there was no information concerning the time of operation. This left 54 cases in our study. In 52 cases it was demonstrated that the onset of the mental illness was prior to treatment of the thyrotoxicosis (51 by thyroidectomy, 1 with radioactive material). The cases are as follows:

Schizophrenic Reactions	27
Involutional Psychotic Reactions	8
Psychoneurotic Reactions	7
Paranoid States	6
CBS with Syphilitic Meningo-encephalitis	2
CBS with Convulsive Disorder	2
CBS with Alzheimer's Disease	1
Manic-depressive Reaction	1
Total	54

From Warren State Hospital.

Case Histories

1. Z.G.P.—This is a 56 year-old white female, married, of the Catholic religion, who came to the W.S.H. December 2, 1953. Her mother died when she was 3. There were 13 children in the family, nine of whom died. The rest were raised by an unmarried maternal aunt who moved into their home. The patient had eight years of schooling. She worked for eight years playing piano in a store and for five years as a telephone operator. She married at the age of 28, to a man of the same age. She was very jealous of her husband and sexual adjustment was very poor. She was rather frigid and sexual frequency was about once every three or four months, possibly due to fear of pregnancy, according to information from her husband. The patient did not allow her daughter to have contact with men and she finally got married without the patient's consent. The patient was never a friendly or social individual, never had close friends, and spent most of her time at home. She had no special hobbies and was considered as being rather quick-tempered.

She began showing signs of mental illness more than twenty years before her commitment and was very seclusive, harboring ideas of infidelity about her husband. She would sit in the farthest corner of a restaurant because she believed people would stare and laugh at her. Due to her anxiety she had a thyroid operation 15 years prior to her commitment. Her recovery was uneventful, but she kept having marked anxiety. Later she became antagonistic toward her neighbors and believed they were laughing at her. Some four years prior to her commitment she thought that police were waiting to arrest her, and a few weeks prior to admission she had an acute episode, thought detectives were all over the home day and night; that neighbors, through dictaphones, were taking down her words; became hallucinated in the auditory sphere, and was taken to the W.S.H. She was diagnosed as a Schizophrenic Reaction, Paranoid Type, and had 30 ECT. After her confusion was over she worked in the occupational therapy program, made a good hospital adjustment, gained insight into her condition, and was released improved February 16, 1954.

2. E.S.—This is a 69 year-old white female, married, of the Protestant religion, who came to the W.S.H. in March, 1954. Early development was said to be normal. She lived on a farm until the age of 14. She had eight years of schooling and was considered a very good student. She married at the age of 23 and marital adjustment was satisfactory. She was described as a serious minded person, not outgoing, very perfectionistic with her housekeeping, and wanted to have everything in its exact place all the time. She was always working

straightening up the house. She did not have special hobbies and all her interests were centered in church activities. She went through her menopause when 50 or 51 years of age, which was around 1935, at which time she was "somewhat jittery and would fly off the handle easily." In 1945 she had a total hysterectomy for prolapse and endometrial polyps. Since 1948 she had complained of dizzy feelings at times, could not stand anything around her neck, and could not exert herself. She was always tired, and felt "just like crying." She was very irritable, excitable and cross most of the time. It was thought she had a hyperactive thyroid and a thyroidectomy was recommended since medication did not help. Before the operation she was withdrawn and quiet. She resisted her hospitalization and thought she was going into a dungeon to be tortured and that she was going to be butchered. In the hospital she suffered a mild convulsion, was extremely nervous, agitated and depressed, but the operation was performed June 18, 1949. Recovery was uneventful, but after her discharge her mental condition became worse. She had paranoid ideation and thought she was going to be punished. She was taken to a mental institution and thought she was going to be electrocuted. She was treated with 21 EST and improved. This did not last and she was in and out of two mental institutions before she came to W.S.H. where she was diagnosed as Involutional Psychotic Reaction. She had 27 ECT and active occupational therapy. Later she became very cheerful, talkative, was not worried, had no bizarre ideation, and was released improved in September 1954.

3. E.H.—This is a 44 year-old white female, married, of the Protestant religion, who came to W.S.H. June 27, 1954. Early development was said to be normal. She was the youngest of five siblings and grew up rather spoiled. The mother died when the patient was 16 years of age. She was graduated as an R.N. and worked two years in private nursing until she was married when she was 25 years of age to a man who was five years her senior. Sexual adjustment was very poor, and the patient practiced masturbation from the age of eight on an average of two or three times a day until four or five years after her marriage. She was fearful of sexual intercourse, was not passionate during the act, and never achieved an orgasm. The husband was impotent and suffered ejaculatio praecox. The medical history revealed an appendectomy at the age of 18, nephritis at the age of 24, and a thyroidectomy in 1937, because of severe anxiety, two years after her marriage. She was described as a fearful individual, very anxious, and a chronic worrier. She was basically serious and conscientious.

Her mental disorder was of insidious onset, and it was felt she was abnormally fearful and worried. Some 11 years prior to her commitment a daughter of 2½ years of age had an injury due to an accident to her neck. Since that time the patient worried a great deal about it but overt psychotic symptoms were observed since early 1954 with marked guilt feelings. She was over-religious and depressed and thought she was being punished by God because of unpardonable sin. She was taken to a mental institution where she received 15 ECT. She improved but this did not last and her former ideas returned. She wept a great deal and finally she was taken to the W.S.H. June 29, 1954, where she was diagnosed as Schizophrenic Reaction, Chronic Undifferentiated Type. She had 20 ECT and active occupational therapy. Her improvement was slow, but she became more cheerful, sociable, and was released November 5, 1954.

4. E.R.—This is a white female, 59 years old, single, of the Protestant religion, who came to W.S.H. July 7, 1954. She was the 6th of 8 children. Early development was said to be normal. Her father had a nervous breakdown when she was six years old, which was quite shocking for her. She was raised on a farm, had had eight years of schooling and made better than average grades. At the age of 14 she had to work as a domestic to help the family and at 23 she attended a business college for three months. After this she worked as a stenographer. She became quite nervous and had to quit work. Subsequently she worked as an attendant in a state hospital and later as a saleslady. Again she became quite nervous and had to stop working because of difficulties with fellow workers and employers. Just before her commitment she was again selling and again had difficulties as before.

She never had a date with a man until she was 24. Then she met an older business executive and she got married secretly. They continued to live separately after the marriage and sexual relations were probably unsatisfactory. She was frightened and had considerable pain. Ten days after the marriage it was discovered that her husband was married to another woman and this was a tremendous shock for the patient. She never saw him again and did not divorce him. When she was 25 years of age she suffered a nervous breakdown. Then she had a feeling of "electricity in my body" and "nerves splitting into a million pieces." She was crying, confused, depressed, and contemplated suicide with carbolic acid. She was taken to a sanitarium and released three months later, improved. At the age of 27 she had a spell of nervousness and depression and it was thought that she had a toxic goiter. Surgery was performed, but an operation did not relieve her nervousness. It made her feel worse. From then on she had frequent similar episodes of less intensity until April of 1954, when after a serious difficulty with employers she became very nervous and confused, was unable to sleep, and felt "in a terrible turmoil." She didn't know what she was doing. Her condition became worse and she had a "heavy feeling in her neck splitting up to the head and the rest of the body." She was also having considerable projection. She came to W.S.H. July 7, 1954, where she was diagnosed as Schizophrenic Reaction, Paranoid Type. She was expected to make a good hospital adjustment without basic

change in her paranoid features of long-standing. She participated in active occupational therapy and was released as improved October 27th of the same year.

Speculation about the dynamics of these cases will not be undertaken due to a lack of refined information in this area and the objective of this article.

Discussion

From our cases 52 out of 54 patients showed the onset of their mental disease definitely prior to the operation. Some type of psychiatric treatment, or diagnostic study at the very least, should be recommended in all patients suspected of having thyrotoxicosis *before* going into major surgery. A trial with ECT would be highly recommended, since this treatment may solve the unconscious conflicting situation which is causing the anxiety, or as Reiss[7] thinks, ECT would bring about the hormone equilibrium between the thyroid activity and the adrenal cortex; or as Selye and Fortier[9] have proposed through "an activation of the pituitary-adrenal axis."

Cases of Thyrotoxicosis in the Warren State Hospital

TABLE I

Distribution of 63 Cases by Sex

Female	85%
Male	15%

TABLE II

Distribution of 54 Cases by Mental Status at Time of Operation

Psychoneurotics	65%
Psychotics	35%

TABLE III

Distribution of 54 Cases by Diagnosis During Admission

Schizophrenias	50.0%
Involutional Psychotic Reaction	14.8%
Psychoneurosis	12.9%
Paranoid States	11.1%
CBS & Epilepsy	3.7%
CBS & Syphilis of CNS	3.7%
CBS & Alzheimer's Disease	1.8%
Manic-depressive Reaction	1.8%

TABLE IV

Distribution of 63 Cases: Rate of Discharge and Retention

Patients discharged improved	63%
Still in the hospital	37%

In Table II it can be seen that the majority of the patients were functioning at a neurotic level before operation, which might have caused sufficient anxiety to simulate a thyrotoxicosis picture; or the same anxiety through hormonal changes may have produced a hyperfunction of the gland. By looking at Table III, it can also be noticed that most of the patients were diagnosed as psychotics during admission; for example, schizophrenia was diagnosed in 50%, which is greater than the proportion of schizophrenics (25-30%) among all hospital admissions. Involutional cases were 14.8% greater than 3.8% of the hospital first admissions, etc., while psychoneurosis was only 12.9%. Also, the rate of discharge (63%) shown in Table IV was lower in the patients who had had a thyroidectomy prior to their commitment, than the average rate of discharge of patients under the age of 65, which is between 78 and 82%. It may be possible that in a neurotic patient the operation, as a traumatic factor, would favor a further regression of their mental process (to a psychotic level, for instance) and act as an obstruction to the recovery from their mental illness. Table I gives an idea of the frequency of the disease in females, which is comparable to figures given by different authors.

Conclusion

Even when it is very difficult to prove either that severe amounts of anxiety, arising from strong conflicting situations, are a factor in the development of thyrotoxicosis; or that anxiety is a part of the symptomatic constellation, there are a number of mental conditions in which the beginning of the disease may be easily confused with toxic goiter. For the patient's benefit a psychiatric study should therefore be part of the differential diagnosis; and in doubtful cases electroshock and other types of psychiatric therapeutic measures should be used before going to major surgical procedures, which are far more risky and expensive.

Summary

Out of all the patients of the W.S.H., 63 were found to have had a thyroidectomy before their commitment. Mental disorders with excessive anxiety may resemble an

early picture of thyrotoxicosis or possibly may produce a hyper-function of the gland. Psychiatric studies are recommended before resorting to major surgical procedures in order to rule out this possibility. Four typical cases are presented.

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Defense and Communication in the Language of Schizophrenia

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Prolonged experience with schizophrenic patients has led me to believe that language is not used by them exclusively for "security operations," that is, "for counteracting their feelings of insecurity among other people," as Harry Stack Sullivan has stated.[1] Actually there seems to be a continuum from pure communication through communication mixed with defense to pure defense. Sometimes the fault for obscure language lies with the patient, sometimes with the listener, sometimes with the nature of the subject matter itself. Most of the material to be presented here is a by-product of group and individual psychotherapeutic efforts made over the past eight years at the Boston State Hospital. It should be emphasized at the outset that much of the language of the schizophrenic remains incomprehensible and probably must remain so if only because of the private nature of subjects referred to by patients and because verbal stimulation of the psychotic may provoke a response appropriate to another or previous situation only remotely similar to the present one.[2] However, the attempt was made to select several examples of language where the meaning, at least for the immediate therapeutic situation, was quite clear. In many cases a stimulus was deliberately introduced which changed the course of the patient's language in an unmistakable fashion, as the examples will show.

Here are two situations taken from group therapy where the meaning and use of the schizophrenic language seemed quite clear. These examples are stated now simply to show the kind of material collected. In one group the leader failed to note references made by patients to the presence of a new recorder. The patients made such remarks as, "A foreigner comes in to take your resources." "Who is he, I'd like to know myself." When these references were allowed to slip by unnoticed, the patients referred to the leader as "Dr. I.Q." One said, "I just love being a human guinea pig." Another said, "I don't like to be treated like a two year-old and feeble-minded. Somebody unbalanced is in charge of the world." In the next meeting of this group following the conference between recorder and leader, references to the recorder were picked up and the patients stopped making nasty remarks.

Another group leader was thrown into a state of anxiety by the presence of a new recorder and saw references to the recorder in

From Boston State Hospital.

everything the patients said. The patients in this group seemed to be less interested in the recorder and more interested in the over-eagerness of the leader. Here is some of the language from that group. "You keep the whole thing crazy on a supposition." "No one is going to do anything wrong to Dr. R." (the recorder). "He is just a subdivision." "Some one is guilty of expansive sin—gluttony is the crime."

Language As Pure Defense

It is well to remember that defense by words may be the end result of a chain of communication failures; that is, the patient may not have heard because of day-dreaming or refusal, he may not have understood for the same reasons, or he may have been unable to understand because of poor education or a literal approach to our language. We may, in other words, have talked over his head and elicited what sounded like a vague or nonsensical reply, such as recitation of the alphabet, or punning on words by their sound.

The language of the schizophrenic as a whole may be used as pure defense, or pure assault, or an attempt to control treatment. When this language ceases to puzzle, control or annoy the therapist, it may immediately be given up. One group leader piqued a patient by putting on and taking off his hat. The patient changed the course of her schizophrenic talk and started to mumble about "waves in the ether," then suddenly caught on to the fact that the leader was needling her instead of vice-versa, dropped her bizarre language and said, "Are you kidding the shirt off my back?" Note how this patient responded in a rather recognizable way to a stimulus which was known to us. This type of response does not always happen so clearly. Most often, one elicits merely a speeding up or a making louder of what the patient is already saying without changing the course of his material.

Language As Mixed Communication And Defense

Quite often the patient wishes to communicate, does so, but in one way or another manages to confuse the listener by adding to a clear statement a "red herring," by using pronouns misleadingly, by changing time and geography, or by referring to remote persons. They utilize these—call them tricks, apparently to defend themselves or to spare the listener's feelings, but communication often does come through. Patients in therapy are quite interested in telling us what is wrong with the therapist's approach with regard to the patient's needs. Here are a few isolated schizophrenic remarks which refer critically to the therapist's activity and understanding during therapy. "Here lies a guy who went five hundred miles an hour dead as a doornail." "Gluttony is the crime." "Your intelligence is so far above anyone that there couldn't be a connection." "You are in New York, we are in Boston." Here is a remark made by a patient who felt she had been ignored (or, we could say, cut dead) by the leader. "Extra—a fellow killed a girl out West. I just saw the headline." And another remark by a patient, "I'd like to go—swimming." The therapist grabbed the bait on that last remark and asked the patient why in the world he wanted to go swimming. Actually the patient seemed tired and restless after a long group meeting and wanted very much to leave the group. The patient may tell what he thinks of us by the use of single words which remotely, by sound association, have another meaning. When a certain patient said, "Yes" to the therapist, she meant (according to her later),[3] "You ass." It is uncanny the way patients make remarks which lie within a blindspot of the therapist. For this reason it is well to have an observer present during group therapy[4] or perhaps the therapist ought to become slightly paranoid!

Language As Communication About Unfamiliar matter

Another difficulty with the language of the schizophrenic stems from the very nature of the subject matter the patient must deal with if he is to discuss his illness at all. The patient has often felt a radical alteration in his personal experience. He has had and maybe is having experiences which are unfamiliar to him at least in the detailed vivid way he is experiencing them. How then is he to communicate such unfamiliar things as the feelings of influence he gets when a domineering man or a lovely woman or his mother enters the room, or a feeling of weak-

ness which is the result of psychological conflict, not muscular exertion. In these situations it is not surprising that the patient says he feels all right but "needs a few egg nogs," or he has the feeling that someone is sucking his blood. It has also been our observation that many of the remarks of schizophrenics are rather straightforward attempts to describe alterations in ego function and feeling. A patient's remark that he feels he is becoming a girl and developing breasts is a description of distortion of his body image. Another patient who says he feels everyone is dead describes a distortion in his image of the other person. Since the ego has many functions including integration of perception, audition and oldfaction, memory, thinking, judging and planning, etc., the possibilities for unusual experiences when these functions are stimulated by anxiety are obviously manifold. Interpretation on this anxiety level is sometimes more helpful to the patient than the attempt to analyze the origin of the words themselves or to regard the patient as regressed to the earlier level before his body image his formed. Dr. Davide Limentani has collected many examples of schizophrenic language that occurred within the general theme of an abnormal mother-child relationship. He mentions the use of such words as "vampire" and "Siamese twins" in this context. Phrases like "empty bag" and "leaking balloon" were used by one of his patients to describe his loss of identity in the so-called symbiotic relationship.[5]

Finally a few miscellaneous remarks which may serve as guides during foggy therapy sessions. In perhaps four out of ten groups one patient emerges as the therapist's particular helper and critic, albeit he is always somewhat obscure in his anxiety to spare his leader's feelings. This is the man to listen to! It is well also to watch for the repetition of language patterns. These patterns may repeat either rapidly or in a slow circle and indicate underlying issues. It is useful to note changes in prevailing imagery—whether increasingly hostile or sexual, and the sheer amount of bizarreness and disorganization, since these changes may be our only clue to the emergence of any troublesome problem in therapy.[6] When this underlying problem—the therapist may have been too inactive or late or imperceptive or provocative of unacceptable feelings—is truly met, the talk becomes clear and the therapist is on familiar language grounds until the next impasse is signaled by some more bizarre language behavior.

I have omitted discussion of another function of psychotic language namely its use for discharge of unbearable tension. This is seen most strikingly in catatonic excitement and has been exemplified in much detail in J. N. Rosen's book "Direct Analysis." Here the language appears to conform closely to the Freudian mechanisms of the dream and to function in a waking dream for the preservation of sanity as the sleeping dream preserves sleep.[7]

In summary, the language of the schizophrenic may be defense, communication mixed with defense, communication about unfamiliar matter or a release from strong tensions. I have tried to add to the literature some relatively clear examples collected from group and individual therapy experiences with schizophrenic patients.

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Book Reviews

LEWIS J. SIEGAL, M.D., LL.B., *Editor*

A TEXTBOOK OF MEDICINE. By Russell L. Cecil, M.D., Sc.D., Professor of Clinical Medicine Emeritus, Cornell University, New York, Robert F. Loeb, M.D., Sc.D., D. Hon. Causa, LL.D., Bard Professor of Medicine, Columbia University, New York, and other Associate Editors. Cloth. $15.00. Pp. 1786. Ninth Edition. W. B. Saunders Company, West Washington Square, Philadelphia, Penna. 1955.

This text book, the first edition of which had originally appeared in 1927 has gone a long way in its forward stride. As one of its landmarks of progress, illustrations first found their place in the text of its fifth edition in 1940. From its 1570 pages in the sixth revision, the present edition contains an increase to 1786 pages. Consistent with the scope of the book, (which admirably covers the field of internal medicine for every work-a-day requirement), some of the material has been re-arranged under section headings which most advantageously provide some framework for the varied grouping of clinical dysfunctions.

Among the subjects not covered heretofore of which there are 39 in this edition, the following few may be mentioned because of their timeliness as well as their clinical importance: nonsyphilitic treponematosis; the leptospiroses; blast injury; war gases; pyridoxine deficiency (as a convulsive causality); delirium (as a disorder of ill-defined boundaries); developmental anomalies of the cervicomedullary juncture. As a random qualitative sampling of the material in the present volume, the subject of barbiturate poisoning may be cited: While rather sketchy in the previous edition, this subject has now been re-authored, and as re-written in the present work, deals in considerable detail with the incidence, etiology, morbid anatomy, pathologic physiology, signs and symptoms, laboratory findings, diagnosis, prognosis, treatment and complications of acute barbiturate poisoning. Of particular significance is the reference to the application of the modulated unidirectional periodic electrocerebral stimulation which which should first be tried and which may thus avoid the necessity for analeptic therapy. With equal precision is also detailed the incidence, patterns of abuse, and all other pertinent elements applicable to the syndromic picture of chronic barbiturate intoxication—barbiturate addiction.

The book, classically continues throughout to emphasize the physiologic, biochemical and psychologic aspects of disease, and discusses each disease entity along these lines wherever consistently possible. The most recent diagnostic and therapeutic advances in medicine are presented throughout the work, and a good deal of the material has been completely revised and some has been newly written by renowned and different contributors. The book continues to be a classic and merits the confidence of the medical student as well as of the practitioner, irrespective of the specialty of his choice.

PERIPHERAL NERVE INJURIES. By Webb Haymaker, M.D., Chief, Neuropathy Section Armed Forces Institute of Pathology, Washington, D.C., and Barnes Woodhall, M.D., Professor of Neurosurgery, Duke University School of Medicine, Durham, N.C. Second Edition, Cloth. $7.00, Pp. 333 with 272 illustrations. W. B. Saunders Company, West Washington Square, Philadelphia, Penna. 1953.

The book which first appeared in a previous edition at the close of World War II in 1945, is presented in its second edition greatly enlarged both as to illustrative and textual material. In this reviewer's opinion the book continues to serve as an authoritative manual in respect of the anatomy, function and methods of clinical examination of the peripheral nervous organization. In my comparison reading of the two editions, I note at once the vast amount of revision which this second edition has received. While it has been brought up to date generally, particular notice should be given to the clarity and repleteness of the analysis of movements tested in the neurological examination where motor deficit is in issue. An entirely new section deals elaborately with the clinicopathological classification of nerve injuries, the selection of appropriate therapy, as well as long-range prognostication. Procaine nerve block as a detector of psychogenicity, of anomalous nerve supply, as a determinant of loss of neurofunction is equally well presented and brought up to date as new matter. As influenced by such varying conditions as time of, and manner of testing, Tinel's sign has received most advanced discussion as to its findings and assessment in the hands of various workers.

References to the applicable literature are profuse throughout the text, in addition to which a liberal bibliography is appended. As a reliable ready reference, the book may be consulted profitably by the neurologist, neurosurgeon, orthopedist, industrial surgeon, technicians in the field of physical therapy and all others concerned with peripheral neurology and its divers pathology.

LEGAL MEDICINE. Edited by R. B. H. Gradwohl, M.D., Sc.D., Director, Police Laboratory, St. Louis Police Department; Pathologist to Christian Hospital. Cloth. $20.00. Pp. 1093, with 222 illustrations. C. V. Mosby Co., 250 Park Avenue, New York, N. Y. 1954.

The book is truly textual and its editor has selected a representative group of collaborators among whom number pathologists, toxicologists, anthropologists, teachers of law and medicine, and law enforcement officials engaged in their respective fields

of the forensic sciences. Each of the contributors has ably demonstrated an expert understanding of the subject under his authorship and the style of the book has been arranged in a manner that reflects creditable editorial acumen to its planner, Dr. Gradwohl.

The material begins with the chapter on the history and development of legal medicine and is traced down to its present advent of twentieth century jurisprudence in our own country. Included in later chapters the student of medicine or law, as well as members of the medical profession, of the bar, and those occupied in ancillary interests, will find the book to further unfold as an authoritative text, in every branch of the forensic sciences. The various chapter subjects are intelligently illustrated by well chosen actual photographs of pertinent cases, include the most advanced methodology respecting tests, examinations, identifications, and discussions of administrative and investigatory aspects, are replete in legal citations, and contain world-wide medical references at the conclusion of each chapter. No single phase of legal medicine has been omitted where medico-legal responsibility is in issue.

The book is written from a truly scientific approach, and while neither space nor readers' time would permit a commentary on each of the chapters, the volume is unusually informative and should be in the hands of every professional person dedicated to the field of forensic medicine.

COUNSELING IN MEDICAL GENETICS. By Sheldon C. Reed, Director of Dight Institute for Human Genetics, The University of Minnesota. $4.00. Pp. 268. W. B. Saunders Company, West Washington Square, Philadelphia, Penna., 1955.

The author makes a valuable contribution to the scientific recognition of genetic traits translatable into a predictable percentage of heritable anomalies within the family constellation. The proponent as the prospective parent, laden with a genetic problem, looks to the physician as the logical medical advisor for help in making a decision respecting proponent's progeny, where heredity as a biologic legacy is the family's concern. It is here that organized professional assistance becomes invaluable to the prospective parent (in fear of repetition of reproduction of next child with abnormality) who is groping for a scientific translation of human genetics in so far as the information may serve to guard him against the possible future risk of reproducing an abnormal offspring—whether the defects be due to environmental, genetic, or a combination of such factors.

The book discusses the implications of medical genetics generally, and elaborates with particularity upon some score of genetic diseases most frequently posed, about which counseling information is expected from the physician. In a discerning manner the author develops the relationship between the genes and Mongolism; interprets the phenomena of such nervous system malformations as anencephaly, hydrocephaly and spina bifida; the sub-recessive genetic background for clubfoot; the variables in the expression of harelip and cleft palate and the peculiar relationship between the age of the mother and its influence upon the occurrence of harelip in the offspring; comparison of, and genetic basis for the occurrence of mental retardation in one-egg (identical) and two-egg (fraternal) twins; major hereditary variation in body bulk; the recessive heredity and consanguinity factor incident to fibrocystic pancreatic disease and its gloomy genetic prognosis; blood genetics; the elusive type of schizophrenic heredity and the random environmental influences incident to its manifestation. The book abounds in illustrative historical examples in the form of queries under each of the problems discussed, and pertinent counselings are exemplified therewith. Notwithstanding its compactness, the book also contains an appendix which lists interpretively an array of other hereditary anomalies, both rare and not so uncommon. The basic principles of medical genetics are scientifically assembled, and the book should serve as a stimulating guide to medical practitioners toward a clearer approach to heredity, the Mendelian laws and their practical application to human genetics.

BOOKS RECEIVED

For readers' attention, books received are descriptively identified. Selected reviews appear in BOOK REVIEW section as space and interest permit.

CLINICAL PSYCHIATRY. By Ian Skottowe, M.D., M.R.C.P., Psychiatrist, Warnerford and Park Hospitals, Oxford; Physician in Charge, Department of Psychiatry, Royal Buckingham Hospital, Aylesbury. Cloth. $8.75. Pp. 395. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York 36, 1954.

DIENCEPHALON. By Walter R. Hess, M.D., Professor of Physiology, Emeritus, University of Zurich. Cloth. Pp. 79. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, 1954.

NEW GOULD MEDICAL DICTIONARY. Cloth. $9.50. Pp. 1294. The Blakiston Company, Inc., 575 Madison Avenue, New York 22, N. Y., 1949.

EMOTIONS AND BODILY CHANGES. By Flanders Dunbar, M.D., Med. Sc.D., Ph.D. Cloth. Fourth Edition. $15.00. Pp. 1192. Columbia University Press, 2960 Broadway, New York 27, N. Y., 1954.

FUNDAMENTALS OF INTERNAL MEDICINE. By Wallace Mason Yater, A.B., M.D., M.S. (In Med.), F.A.C.P. Director, Yater Clinic, Washington, D.C. Cloth. $13.50. Fourth edition. Pp. 1306, with illustrations. Appleton-Century-Crofs, Inc., 35 West 32nd Street, New York 1, N. Y., 1954.

TEXTBOOK OF THE NERVOUS SYSTEM. By H. Chandler Elliott, M.A., Ph.D. Cloth. $9.00. Second edition. Pp. 437, with illustrations. J. B. Lippincott Company, East Washington Square, Philadelphia 5, Penna., 1954.

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